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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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Robert John Noel

MCA-609 US

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EXAMINER

SAUNDERS, DAVID A

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**Please find below and/or attached an Office communication concerning this application or proceeding.**

The time period for reply, if any, is set in the attached communication.

<b>Office Action Summary</b>	<b>Application No.</b> 10/521,730	<b>Applicant(s)</b> NOEL, ROBERT JOHN	
	<b>Examiner</b> David A. Saunders	<b>Art Unit</b> 1644	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

### Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

### Status

- 1) ☒ Responsive to communication(s) filed on 02 October 2009.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

### Disposition of Claims

- 4) ☒ Claim(s) 1-3,5,7-16,18 and 19 is/are pending in the application.
- 4a) Of the above claim(s) \_\_\_\_\_ is/are withdrawn from consideration.
- 5) ☒ Claim(s) 15,16 and 18 is/are allowed.
- 6) ☒ Claim(s) 1-3,5,7-14 and 19 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

### Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

### Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some \* c) ☐ None of:
- ☐ Certified copies of the priority documents have been received.
  - ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
  - ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

### Attachment(s)

- |   |   |
|---|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892)                    | 4) <input type="checkbox"/> Interview Summary (PTO-413)           |
| 2) <input type="checkbox"/> Notice of Draftperson's Patent Drawing Review (PTO-948) | Paper No(s)/Mail Date. _____                                      |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08)         | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| Paper No(s)/Mail Date _____   | 6) <input type="checkbox"/> Other: _____                          |

### **AMENDMENT ENTRY**

Amendment of 10/2/09 has been entered. Claims 1-3, 5, 7-16 and 18-19 are pending and are under consideration.

### **CORRECTIONS REGARDING PREVIOUS OFFICE ACTION**

The following corrections pertain to the previous Office action:

At page(s) 10, line 6 “1417” should have read as – 14-17 --.

### **OBJECTION(S)/REJECTION(S) OF RECORD WITHDRAWN**

The amendment has overcome previously stated issues as follows:

The objection to claim 6 under 37 CFR 1.75, since claim 6 has been cancelled.

The rejection of claim(s) 1 and 5 under 35 USC 112, 2<sup>nd</sup> paragraph for inconsistent recitations.

The rejection of claim(s) 1, 12 and 15 under 35 USC 112, 2<sup>nd</sup> paragraph, for recitation of “in the absence of an added salt...” This phrase has been deleted from all independent claims.

The rejection of claim(s) 1-3 and 5-20 under 35 USC 112, 1st paragraph, for recitation of “in the absence of an added salt...” This phrase has been deleted from all independent claims.

The rejection of claim(s) 1-3 And 5-20 under 35 USC 112, 1st paragraph, for failure to disclose the best mode. The fact that Applicant has provided a conductivity range for the buffer used in Example 1 would permit one to calculate the permissible

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range and/or upper limit of concentration for a positive charged ion that can bind to the matrix/adsorbent.

The rejection of claim(s) 20 under 35 USC 112, 1st paragraph for new matter, since claim 20 has been cancelled.

The rejection of claim(s) 19-20 under 35 USC 112, 1st paragraph regarding the enablement for binding "only the selected ionic polymeric compound". Claim 20 has been cancelled; and the rejection of remaining claim 19 has been overcome, due to changes introduced into base claim 15.

The prior art rejection of claim(s) 12 and 15-16 based upon Scholz et al, since each of claims 12 and 15 presently recite an ionic charge density range. The reference does not state the ligand density of any of the adsorbents studied. The adsorbents of this reference were prepared in the authors' own laboratory (pp 190-192). There is thus no standard reference which one could consult in order to determine what might be the inherent ligand density of any of the adsorbents.

The prior art rejection of claim(s) 15-17 and 19 based upon Lihme et al. The reference does not teach separating protein-A from immunoglobulin G.

The prior art rejection of claim(s) 15-16 based upon Hahn et al. The reference does not teach separating protein-A from immunoglobulin G.

The 102/103 rejection of claim(s) 1, 5-6, 9-12 and 15-16 based upon Reithorst et al, who do not teach use of cation exchangers.

The prior art rejection of claim(s) 15-19 based upon Graf et al. The reference does not teach separating protein-A from immunoglobulin G.

### **NEW OBJECTION(S) TO CLAIMS**

Claim 2 is objected to under 37 CFR 1.75(c), as being of improper dependent form for failing to further limit the subject matter of a previous claim. Applicant is required to cancel the claim(s), or amend the claim(s) to place the claim(s) in proper dependent form, or rewrite the claim(s) in independent form. Claim 2 fails to further limit claim 1, since claim 1 has been amended to limit the adsorbent to a "cation-exchange adsorbent".

Claim 9 is objected to under 37 CFR 1.75(i), as being of improper format for failing to indent step c).

### **NEW REJECTION(S) UNDER 35 USC 112, SECOND PARAGRAPH**

Claim(s) 1-3, 5 and 7-14 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

In claim 1, line 10 "the cation-exchange adsorbent" lacks antecedent basis, because claim 1, line 2 recites a "selective cation-exchange adsorbent".

In claim 1, last line "the selective ionic adsorbent" lacks antecedent basis, because claim 1, line 2 recites a "selective cation-exchange adsorbent".

In claim 2, "the selective ionic adsorbent" lacks antecedent basis, because base claim 1, line 2 recites a "selective cation-exchange adsorbent".

In claim 5, line 3 and in claims 10-11, line 2 of each, "the selective cation-exchange ionic adsorbent" lacks antecedent basis, because base claim 1 recites a "selective cation-exchange adsorbent".

Claim 12, at lines 3 and 7, refers to a "selective cation-exchange adsorbent" and subsequently refers to "the cation exchange adsorbent". Dependent claims 13-14 also refer to "the cation exchange adsorbent". Consistent terminology is required.

**NEW REJECTION(S) UNDER 35 USC 112, FIRST PARAGRAPH**

Claim 19 is rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. Applicant has not described a “sample component” in accord with the limitations of claim 19.

Specifically, base claim 15 has been amended such that the sample is one containing a “protein-A component” and an “immunoglobulin G component”. Applicant has not described how a “protein-A component” would be one normally found in a blood sample or cell culture broth. Indeed, one of skill would contemplate that a “protein-A component” might be present, along with an “immunoglobulin G component” for the case in which the sample is one containing IgG eluted from a protein-A affinity adsorbent column (due to the presence of leached protein-A in the eluent). Such an eluted “sample”, however, might be processed from a blood sample or cell culture broth, but it would not constitute a blood sample or cell culture broth, per se.

**MAINTAINED REJECTION(S) UNDER 35 USC 102 OR 102/103**

Claims 1-2 and 9-11 are rejected under 35 U.S.C. 102(b) as being anticipated by Wu et al.

Wu show experiments in which they prepare various, individual protein solutions, each in a buffer of 0.01M (10 mM) sodium phosphate. Wu et al then apply samples of each of these protein solutions to each of a series of carboxylate cation-exchangers/adsorbents having different carboxylate ion (ligand) densities, such that the proteins are adsorbed to each of the exchangers. At a carboxylate ligand density of 70 umol/g the exchanger/adsorbent starts to become saturated with protein (e.g. lysozyme). See pgs 8-10 and Fig. 2.

Instant claims 1 and 2 are anticipated since claim 1 has been amended such that one merely needs to bind a protein to the cation exchange adsorbent and thereby

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separate the protein from a "sample component". In this case the Office is interpreting the "sample component" to be merely the solution of the individual protein in the 10 mM sodium phosphate buffer. This interpretation of what is meant by a "sample component" is proper, since applicant has used the phrase "sample component" to refer to an even more complex mixture containing the ionic protein component of interest. For example, note claim 19, which recites "wherein the sample component is selected from the group consisting of blood and cell culture broths."

Wu et al then elute the adsorbed protein from each of these cation exchangers, by varying sodium sulfate concentration in the 10 mM sodium phosphate buffer (See Fig. 4); thus claim 9 is anticipated.

Applicant's arguments filed 10/2/09 have been fully considered but they are not persuasive. Applicant has urged (p 11) that the reference cannot be applied, because Wu et al bind the ionic component (e.g. lysozyme) to the cation-exchange adsorbent in the presence of one or two additional ionic components that also bind to the adsorbent (e.g. a Na<sup>+</sup> salt) in either solution A or B. This argument is unfounded because it pertains to a previously recited claim limitation, that has now been deleted from Claim 1. Furthermore, the Office considers that salt from a buffer can be present in/added to the sample, since applicant's own teachings in Example 1 include the addition of a buffer to the sample.

Claims 1-2, 5, 7 and 9-14 are rejected under 35 U.S.C. 102(a), (b) or (e) as being anticipated by Lihme et al (US 6,498,236 or WO 98/08603).

The US and foreign references have the same disclosure. The rejection is based upon 102 (a)/(e) for the former and under 102 (b) for the latter. For convenience the examiner will refer to the US document by col. and line number.

Lihme et al teach chromatographic adsorbents/matrices which have a negative charge on their surface, due to the presence of a COOH group attached to an aromatic ring. This group would be ionized at the taught pK range values for the COOH group and the taught pH ranges values for adsorption (e.g. see col. 8, lines 46-65 and col. 15,

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lines 25-41). For the exemplified 2-mercaptobenzoic acid (2-MBA), the pH values at which binding of immunoglobulins occurs are in the acid range, where the COOH group would be ionized (e.g. col. 31, lines 27-59). For the exemplified 2-amino-benzoic acid (4-ABA), the pH values at which binding of immunoglobulins occurs are in the acid range, where the COOH group would be ionized (e.g. col. 35, lines 1-52). For the exemplified 2-mercapto-nicotinic acid, the pH values at which binding of immunoglobulins occurs are in the acid range, where the COOH group would be ionized (e.g. col. 36, lines 1-50). The operative and exemplified ligand densities are taught at col. 18, lines 17-32; col. 30, lines 29-34; col. 34, lines 62-67; col. 35, lines 62-65; col. 38, line 31; and col. 39, line 39.

The exemplified separations of IgG from an "Artificial Culture Supernatant" (col. 30, lines 30+) and from sera (col. 38, lines 9+) most certainly show a separation in which a "first ionic protein compound of interest" in a sample binds to the adsorbent and a "second different ionic protein compound" (e.g. one or more proteins in the fetal calf serum of the "Artificial Culture Supernatant") in a sample does not bind to the adsorbent, as in instant claim 12. This exemplification is also consistent with the case in which a "selected ionic protein compound of interest" binds to the adsorbent and a "sample component" (e.g. one or more proteins in the fetal calf serum of the "Artificial Culture Supernatant") does not bind to the adsorbent, as in instant claim 1.

From the above instant claims 1-2, 5, 7 and 10-14 are anticipated.

For claim 9, note that Lihme et al elute the adsorbed IgG (e.g. col. 4, lines 30-33; col. 7, lines 19-47; col. 30, lines 56-61; col. 32, lines 19-61; col. 35, lines 31-53).

Applicant's arguments filed 10/2/09 have been fully considered but they are not persuasive. Applicant has generally asserted (p 14) that the reference does not meet all the limitations recited in claims 1 or 12; however, applicant has failed to point out exactly which limitations of claims 1 or 12 have not been met.



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Claims 12-14 are rejected under 35 U.S.C. 102(b) as being anticipated by or, in the alternative, under 35 U.S.C. 103(a) as obvious over Hahn et al (Jour. Chromat. A., 795, 277-287, 1998).

This rejection of record has been maintained for independent claim 12 and extended to amended dependent claims 13-14.

Hahn et al show a sample of bovine whey. The whey is prepared by addition of HCL to milk, in order to precipitate casein, which is then removed by centrifugation. The thus obtained whey is diluted with water to a conductivity of 2.7 mS/cm. The Office sees such preparation of whey as indistinguishable from that exemplified by applicant (Example 2). See Hahn et al at para. spanning pp 278-279.

The thus prepared whey is then contacted with one of various cation-exchange resins, including S-Sepharose FF (p 278, col. 2), under conditions such that IgG bound to the adsorbent and alpha-lactalbumin passes through the column (para. spanning pp 280-281). Thus there is a separation in which a "first ionic protein compound of interest" in sample binds to the adsorbent and a "second different ionic protein compound" in a sample does not bind to the adsorbent.

While the reference does not teach the charge density of the S-Sepharose FF employed, it is taken that it must have been the same as or close to that that having a charge density of 75 umol/ml that was used by applicant in Example 2. Otherwise, there would have been no selective binding of the IgG. Hence, instant claims 12-14 are anticipated or, at the least, obvious.

Applicant's arguments filed 10/2/09 have been fully considered but they are not persuasive. While Applicant has urged (p 15) that the reference does not meet all the limitations recited in claim 12, the Office considers that the charge density of the S-Sepharose FF employed by Hahn et al must have been the same as or close to the charge density of 75 umol/ml exemplified by applicant in Example 2, since Hahn and applicant both differentially adsorbed whey proteins to the S-Sepharose FF.

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Claims 1-2, 5, 7, 9 and 12 are rejected under 35 U.S.C. 102(b) as anticipated by or, in the alternative, under 35 U.S.C. 103(a) as obvious over Graf et al (Bioseparation, 4, 7-20, 1994).

Graf et al teach various ion exchange matrices/adsorbents for the separation of a monoclonal antibody from an animal cell culture fluid. The ueq/ml values given in Table 1 correspond to the umol/ml values recited in the instant claims. Therein SP Sepherodex M (a cation exchanger) has a binding capacity of 100 ueq/ml (upper end of range recited in instant claims 1 and 12). For the case of using a cation exchanger, the majority of the monoclonal antibody present in the animal cell culture fluid sample binds to the exemplified columns, and "most of the contaminant proteins are removed in the flow through fraction" (p 12, col. 2). Thus there is selective binding of monoclonal antibody to the matrices/adsorbents.

From the above, instant claims 1-2, 5, 7, 10 and 12 are anticipated or obvious.

Regarding dependent claim 9, Graf et al elute the adsorbed antibody (p 12, col. 1-2).

The examiner considers that the claims are anticipated; however, an obviousness rejection is made in the alternative (e.g. in the event that applicant should argue the limits of the recited charge density ranges in relation to the ueq/ml values taught by Graf et al).

Applicant's response of 10/2/09 did not traverse the rejection over Graf et al.

## **FINALITY**

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire **THREE MONTHS** from the mailing date of this action. In the event a first reply is filed within

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TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

## **CONTACTS**

Any inquiry concerning this communication or earlier communications from the examiner should be directed to David A. Saunders, whose telephone number is 571-272-0849. The examiner can normally be reached on Mon.-Thu. from 8:00 am to 5:30 pm and on alternate Fridays. The examiner's supervisor, Ram Shukla, can be reached on 571-272-0735. The fax number where this application is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Typed 3/15/10 DAS

/David A Saunders/

Primary Examiner, Art Unit 1644